

**Figure 1A**

**NOVTRAN cDNA sequence:**

atgcagtggctcctgtctggcctgtacctcctcagggctctccacatgtcctgtctctctgagagacctgtgcctgtgcccacagggaccaagctcttc  
cactcctgtatcacctcaacgaacccatgcgcctcctcctggaggtgtgtgtgaagctgcaggcatcacccctggactgtagggtctgagcacccgcc  
ctgtccatcatccctgcatgcctctccgttcaccgactcctcaacagaccatccctgtcctctcaacaggccccgctctgtctggggaacca  
cggacagaggccttcccatccccaggcctgaaggccagagtaggtgggaccatctcgcgaagccggcctcaattctcaaggccatgccgtggagc  
cagtgccatctggaccctctgggtcaagcaaagggtgtgtgctaatcaaaaggcagccctcgaggatgccaaaggccccggaatgccagtggaccg  
tgaaaaccttctgtgacaaacctgcagtgccttctctgtccagctgtctccagctctccatgcatcaagggtggaacagagcaggagcgcagtaatg  
cggaaattgacttgcaaagtcgggcccgtcgggattacaattcaaggctgtctgtgaaactcgggcagatccagctgcaaagggcagttccttctcga  
gtgcagaacgtgtctggagggttggctcagcccagggtcccaggaaccactgcaagggtggggcgggccctcagagcccttccagagctggg  
ggctggtagcccccttggcttggagaaggtcagtacccaacccatccccaggcccagctcggaagggtgtggaactggccccctgtgtctctgt  
gaccagtgtccactgtgcactctccaggccagccgaacctggcacacactgggtgttccctaaatagccatggagggtattgtggcatggagagctgtc  
gattccagaaacctcctggacatagggtgggagctcatctgcagaagctgcctga

**Figure 1B**

**NOVTRAN Protein Sequence:**

MQWSCLACTLLRVLPVLSLLRDPVPVPTGTKLFHSCITSTNPCASFLEVAVEAAGITPW  
TVGSEHPPCPYPYPSLHASPFDTDSFNRPSPAPLNRPRSAGEPRTEAFPSPGLKARVGGTILAE  
AGLNSQGHAVEPVPSGPSGSSKGCVLIKGRPSRMPKARECPVDRENLLLTPNAVPSLLQL  
LSSSPCIKVETEQUERSNAEFDLQSRARDYNSRLLLKLGQIPAAKGSSFLELQNVSGGVG  
SARGPRNHCKVGAGPQSPFPELGAGSPPLALEKVSTQPIQARLRKGVDWPPVSPGDQC  
PLCTLPGQPNLAHTGCSLNSHGGYCGMESCRFQKPPGHRAGSSSAEAA

## Figure 2A

### BlastN for NOVTRAN:

gb:GENBANK-ID:H55724|acc:H55724 CHR220663 Chromosome 22 exon Homo sapiens  
genomic clone C22\_916 5', mRNA sequence - Homo sapiens, 171 bp.

Minus Strand HSPs:

Score = 585 (87.8 bits), Expect = 1.0e-19, P = 1.0e-19  
Identities = 117/117 (100%), Positives = 117/117 (100%), Strand = Minus /  
Plus

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Query:    735 ACCTCGGGCTGAGCCAAACCCCTCCAGACACGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 676
          |||
Sbjct:    18  ACCTCGGGCTGAGCCAAACCCCTCCAGACACGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 77

Query:    675 TGCAGCTGGGATCTGCCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 619
          |||
Sbjct:    78  TGCAGCTGGGATCTGCCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 134
```

Figure 2B

**BlastX for NOVTRAN:**

No Hits:

ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18...	-3	102	0.0093	1
ptnr:SPTREMBL-ACC:Q26876 PROTECTIVE RECOMBINANT ANTIGE...	-3	87	0.018	1
ptnr:TREMBLNEW-ACC:AAD41775 PRO-ALPHA-2(I) COLLAGEN - ...	-3	86	0.061	2
ptnr:PIR-ID:S46272 anther-specific protein - common su...	-3	94	0.073	1
ptnr:SPTREMBL-ACC:Q26874 PROTECTIVE RECOMBINANT ANTIGE...	-3	78	0.16	1
ptnr:SPTREMBL-ACC:Q92029 ALPHA-1 COLLAGEN TYPE III - G...	-3	86	0.19	3
ptnr:SWISSPROT-ACC:P46804 SPIDROIN 2 (DRAGLINE SILK FI...	-3	101	0.24	1
ptnr:SPTREMBL-ACC:O57808 103AA LONG HYPOTHETICAL PROTE...	+2	76	0.25	1
ptnr:SWISSNEW-ACC:P41484 PROLINE-RICH ANTIGEN (36 KD A...	-3	95	0.26	1

**CuraBLASTX Analysis of AC007663\_A**

PUBLIC DATABASE

Query= AC007663\_A Cura\_109 transmembrane protein  
(1047 letters)

Database: /opt/database/public/blast/protnr  
577,633 sequences; 178,813,065 total letters.

		Reading	High	Smallest	
		Frame	Score	Sum	
Sequences producing High-scoring Segment Pairs:			Probability	P(N)	N
ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18...	-3	102	0.015	1	
ptnr:pir-id:S12246 anther-specific protein SF18 precur...	-3	102	0.015	1	

PATENT DATABASE

**CuraBLASTX Analysis of AC007663\_A**

Query= AC007663\_A Cura\_109 transmembrane protein  
(1047 letters) of query sequence in all 6 reading frames

Database: /opt/database/licensed/blast/geneseq\_aa  
349,121 sequences; 51,277,408 total letters.

		Reading	High	Smallest	
		Frame	Score	Sum	
Sequences producing High-scoring Segment Pairs:			Probability	P(N)	N
patp:R28916 Type III procollagen (prior art) - Homo sa...	+1	81	0.059	3	
patp:W03454 Mutant mouse c-AKT non-translation region ...	+1	81	0.075	1	
patp:G04146 Arabidopsis thaliana protein fragment SEQ ...	-3	80	0.095	1	

### Figure 3A

#### NOVNEUR cDNA sequence:

Regions 135319 to 135129 (1-190bp) and 134487 to 134314 (191 to 364bp) of the genomic clone (in - frame). Further extended using ESTs AI739078, AI767488, and AI796217.

AGCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCATGGCCCGCGGGAGGGCGCTCGGATGTTTCGGC  
AGCCTCCTGCACTTCGCCCTGCTCGCTGCCGGCGTCGTCCCGCTCAGCTGGGATCTCCCGGAGCCCCGCA  
GCCGAGCCAGCAAGATCCGAGTGCCTCGCGAGGCAAGCTCTGGGCCATCGGTCAC'TTCATGGGCAAGAA  
GAGTCTGGAGCCTTCCAGCCCATTCCCATTTGGGGACAGCTCCCCACAGCTCCCTGAGGGACCAGCGACTG  
CAGCTGAGTCATGATCTGCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCG  
CACCCCAAATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATGGGGCAGACA  
CAACAGCGTGGCTTAGATTGTGCCCCACCCAGGGAAGGTGCTGAATGGGACCCTGTTGATGGCCCCATCTG  
GATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATTTCTGGCTGGGTCAACAGAAATATC  
GCTGATGCAGACACAGATTATGTTCTCTGCTGTATTTCTCTGCTTCCCTGTTGAATTGGTGAATAAAACCTT  
GCTCTATACATACAAA

### Figure 3B

#### NOVNEUR Protein sequence:

MFGSLLHFAALLAAGVVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLEPSSPSPLGTAPHTSLRDQRLQLSH  
DLGILLKKALGVSLSRPAPQIQYRLLVQILQK

Figure 4A

**BlastN for NOVNEUR:**

gb:GENBANK-ID:HUMNKB|acc:M21551 Human neuromedin B mRNA, complete cds -  
Homo sapiens, 640 bp (RNA).

Top Previous Match Next Match  
Length = 640

Plus Strand HSPs:

Score = 3055 (458.4 bits), Expect = 9.1e-132, P = 9.1e-132

Identities = 629/639 (98%), Positives = 629/639 (98%), Strand = Plus / Plus

```

Query:      2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC-ATGGCCCG-CGG-CGGGAGGGCGCT 58
             GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC ATGGCCCG CGG CGG GGGCGCT
Sbjct:      2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCCATGGCCCGCGGGCGGG-GGGCGCT 60

Query:     59 CGGATGTTTCGGCAGCCTCCTGCACCTTCGCCCTGCTCGCTGCCGGCGTCTGTCCTCCGCTCAGC 118
             CGGATGTTTCGGCAGCCTCCTGC CTTGCCCTGCTCGCTGCCGGCGTCTG CCGCTCAGC
Sbjct:     61 CGGATGTTTCGGCAGCCTCCTGCCTCTTCGCCCTGCTCGCTGCCGGCGTCTGCCCCGCTCAGC 120

Query:    119 TGGGATCTCCCGGAGCCCCGCGAGCCGAGCCAGCAAGATCCGAGTGCACCTCGCGAGGCAAG 178
             TGGGATCTCCCGGAGCCCCGCGAGCCGAGCCAGCAAGATCCGAGTGCACCTCGCGAGGCAA
Sbjct:    121 TGGGATCTCCCGGAGCCCCGCGAGCCGAGCCAGCAAGATCCGAGTGCACCTCGCGAGGCAAC 180

Query:    179 CTCTGGGGCCATCGGTCACTTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCCCA 238
             CTCTGGGGCA CGGTCACTTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCC A
Sbjct:    181 CTCTGGGGCCACCGGTCACTTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCC-A 239

Query:    239 TTGGGGACAGCTCCCCACACCTCCC-TGAGGGACCAGCGACTGCAGCTGAGTCATGATCT 297
             TTGGGGACAGCTCCCCACACCTCCC TGAGGGACCAGCGACTGCAGCTGAGTCATGATCT
Sbjct:    240 TTGGGGACAGCTCCCCACACCTCCCCCTGAGGGACCAGCGACTGCAGCTGAGTCATGATCT 299

Query:    298 GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCCA 357
             GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCCA
Sbjct:    300 GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCCA 359

Query:    358 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT-GGGGCA 416
             AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT GGGGCA
Sbjct:    360 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATAGGGGCA 419

Query:    417 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT 476
             GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT
Sbjct:    420 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT 479

Query:    477 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 536
             GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT
Sbjct:    480 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 539

Query:    537 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT 596
             TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT
Sbjct:    540 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT 599

Query:    597 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTAT 637
             CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCT T
Sbjct:    600 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTTT 640

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## Figure 4B

### BlastX for NOVNEUR:

ptnr:SWISSPROT-ACC:P08949 NEUROMEDIN B-32 PRECURSOR [CONTAINS: NEUROMEDIN B] - Homo sapiens (Human), 121 aa.

Top Previous Match Next Match

Length = 121

Plus Strand HSPs:

Score = 513 (180.6 bits), Expect = 1.9e-48, P = 1.9e-48

Identities = 105/118 (88%), Positives = 105/118 (88%), Frame = +2

Query: 44 RREGARMFGSLLHFALLAAGVVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLEP 223  
R GARMFGSLL FALLAAGV PLSWDLPEPRSRASKIRVHSRG LWA GHFMGKKSLEP  
Sbjct: 4 RAGGARMFGSLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKSLEP 63

Query: 224 SSPSPGLTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLLVQILQK 397  
SSPS G P LRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLLVQILQK  
Sbjct: 64 SSPSHWGQLPTPPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLLVQILQK 121

Figure 5

ClustalW for NOVNEUR:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g., L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) A37178 (neuromedin B precursor + rat): Locus A37178, accession A37178, PID - g112182
- 2) NEUB\_HUMAN (NEUROMEDIN B-32 PRECURSOR): Locus - NEUB\_HUMAN, accession - P08949, PID - g1346684

```
Neuromedin_New_REVCOMP  -----MFGSLLHFAALLAAGVPLSWDLPEPRSRASKIRVHSRGKLWALGHFMGKKS
A37178                  MTRQAGSTWLLRGLLLFALEFVSGITPFSWDLPEPRSRASKIRVHPRGNLWATGHFMGKKS
NEUB_HUMAN              MARRAGGARMFGSLLLFAALLAAGVPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Neuromedin_New_REVCOMP  LEPSSPSPLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQIL●
A37178                  LEPPSLSLVGTAPPITQREQRLQLSHDLLRIILLQKALGMNLSGPAPPIQYRRLLOK---
NEUB_HUMAN              LEPSSPSHWGQLPTPPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLV●ILQ

Neuromedin_New_REVCOMP  K
A37178                  -
NEUB_HUMAN              K
```

### Figure 6A

#### NOVGON cDNA sequence:

1  
ATGAAGCTGGCATTCCCTCTTCCTTGGCCCCATGGCCCTCCTCCTTCTGGCTGGCTATGGCTGTGTCCTCGGTGCCTCCAG  
81  
TGGGAACCTGCGCACCTTTGTGGGCTGTGCCGTGAGGGAGTTTACTTTCCCTGGCCAAGAAGCCAGGCTGCAGGGGCCTTC  
161  
GGATCACCAÇGGATGCCTGCTGGGGTCGCTGTGAGACCTGGGAGAAAÇCCATTCTGGAACÇÇÇÇCTATATTGAAGÇÇÇAT  
241  
ÇATCGAGTCTGTACCTACAACGAGACÇAAACAGGTGACTGTCAAGCTGCCCAACTGTGÇÇÇÇGGGAGTCGACÇÇÇTTCTA  
321  
CACCTATÇÇÇÇTGGCCATÇÇÇCTGTGACTGÇGGAGCCTGCTÇCACTGCCACCAÇGGAGCTGAGGTTGATGCCAGGGGAAG  
401  
CTGCTGTGGCACTGGGCTTCTGGTGTÇAGCGTAGGAGACAGGGATCTAGGACAACAGGGACCAGGTGGCGACATGCAGCT  
481  
GTAAGAGACAAGGTGAGTCTCCTGAAGGCAGTAGATGGTTGGAATGGGCTGCTTGGGGACCCAGCGAGCTCCÇAGGGCCT  
561  
TTCTGCTTCTTCCGTGTACÇÇÇTGTATTTCCCTTGGCTTTCCAAATTGACTCAGCTTCTGGTAAAGTTGGAAACTTTTCCA  
641  
GCAAACAGACCTTCATCTTCTCCAGTGCAGAGATTACATTAGGAGGAACATGA

### Figure 6B

#### NOVGON Protein Sequence:

MKLAFLFLGPMALLLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCRGLRITTD  
CWGRCEWKEPPYIEAHHRVCTYNETKQVTVKLPNCAPGVDPFYTYPVAIRCDG  
ACSTATTELRLMPGEAAVALGFWCQRRRQGSRTTGTRWRHAAVRDKVSLLKAVDGW  
NLLGDPASSQGLSASSCTPVFPLAFQIDSASGKVGNFSSKQTFIFSSAEITLGGT\*



## Figure 7A

### BlastN for NOVGON:

AF146151 Salmo salar gonadotropin II beta subunit mRNA,  
partial cds - Salmo salar, 266 bp (RNA).

Top Previous Match Next Match  
Length = 266

#### Plus Strand HSPs:

Score = 208 (31.2 bits), Expect = 0.043, P = 0.042

Identities = 124/205 (60%), Positives = 124/205 (60%), Strand = Plus / Plus

Query: 177 CTGCTGGGGTCGCTGTGAGACCTGGGAGAAACCCATTCTGGAACCCCCCTATATTGAAGC 236

CTGC G GG C CTG G ACC GGAG CC TT T AA CCC AT TT A C

Sbjct: 34 CTGCAGTGGCCACTGCGTCACCAAGGAG---CCGGTTTTTC-AAGAGCCC-ATTTTCCACC 88

Query: 237 CCAT-C-ATCGAGTCTGTACCTACAACGA-GACCAAACAGGTGACTGTCAAGCTGCCCCAA 293

T C A C GT TG ACCTAC GA G CC A G AC TC CT CC A

Sbjct: 89 GTGTACCAGCATGTGTGCACCTACCGGGACGTCCGCT-ATGAAACGATCCGCCTACCTGA 147

Query: 294 CTGTGCCCCGGGAGTGGACCC-CTTCTACACCTATCCCGTGGCCATCCGCTGTGACTGCG 352

CTGT CCCC G GT GACC C T T CACCTA CC GTGGC T GCTGTGACTGC

Sbjct: 148 CTGTCCCCCTTGGGTGGACCATCATGT-CACCTACCCTGTGGCTCTGAGCTGTGACTGCA 206

Query: 353 GAGCCTGCTCCACTGCCACCACGGAGCTG 381

G CTG CA G CAC C GA CTG

Sbjct: 207 GCCTCTGTAACATGGACACTTCTGA-CTG 234

## Figure 7B

### BlastX for NOVGON:

P01235 GONADOTROPIN BETA CHAIN PRECURSOR - *Cyprinus carpio* (Common carp), 144 aa.

Score = 203 (71.5 bits), Expect = 2.3e-16, P = 2.3e-16  
Identities = 37/85 (43%), Positives = 52/85 (61%)

Query: 42 TFLAKKPGC-RGLRITTDACWGRCEWKEPILEPPYIEAHHRVCTYNETKQVTVKLPNCA 100  
T +K GC + L + T C G C T E P+ + P+ + VCTY + + TV+LP+C  
Sbjct: 39 TVAVEKEGCPKCLVLQTTICSGHCLTKE-PVYKSPFSTVYQHVCITYRDVRYETVRLPDCP 97

Query: 101 PGVDPFYTYTPVAIRCDGACSTATTE 126  
PGVDP TYPVA+ CDC C+ T++  
Sbjct: 98 PGVDPHITYPVALSCDCSLCTMDTSD 123

>ptnr:SWISSNEW-ACC:Q9YGH2 GONADOTROPIN BETA-II CHAIN PRECURSOR (GTH-II-BETA)  
- *Clupea pallasii* (Pacific herring), 149 aa.  
Plus Strand HSPs:

Score = 206 (72.5 bits), Expect = 1.0e-15, P = 1.0e-15  
Identities = 47/117 (40%), Positives = 63/117 (53%), Frame = +1

Query: 28 PMALLLLAGYGCVLG--ASSGNLRTFVGCAVREFTFLAKKPGC-RGLRITTDACWGRCEWKE 198  
P +LL CVL A NL+ C + T +K GC R L T C G C T  
Sbjct: 5 PECTILLLLCMCVLAVPAQCFNLQP---CVLVNETVSVEKEGCPRLVFRITICSGHCPT 61

Query: 199 WEKPILEPPYIEAHHRVCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378  
E P+ + P+ + VCTY + T++LP+CA GVDP TYPVA+ C+C CS T++  
Sbjct: 62 KE-PVYKSPFSVNVQHVCITYGNFRYETIRLPDCADGVDPVLTYPVALSCECSLCSMDTSD 120

>patp:R15106 hCG/bLH chimera, D10 - *Homo sapiens*, 145 aa.  
Plus Strand HSPs:

Score = 188 (66.2 bits), Expect = 5.0e-14, P = 5.0e-14  
Identities = 40/101 (39%), Positives = 58/101 (57%), Frame = +1

Query: 76 SSGNLRTFVGCAVREFTFLAKKPGCRG-LRITTDACWGRCEWKE--PILEPPYIEAHHR 246  
S G LR C T A+K C + TT C G C + ++ P++ PP + R  
Sbjct: 1 SRGPLRPL--CQPINATLAAEKEACPVCTITFTTSICAGYCPSMKRVLPVILPPMPQ---R 55

Query: 247 VCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378  
VCTY+E + +V+LP C PGVDP ++PVA+ C CG C ++T+  
Sbjct: 56 VCTYHELRFASVRLPGCPPGVDPMVSPVALSCHCGPCRLSSTD 99

>patp:W65110 Equine chorionic gonadotropin beta-chain protein - *Equus caballus*, 169 aa.  
Plus Strand HSPs:

Score = 175 (61.6 bits), Expect = 1.2e-12, P = 1.2e-12  
Identities = 43/116 (37%), Positives = 60/116 (51%), Frame = +1

Query: 31 MALLLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCR-GLRITTDACWGRCEWKE 207  
+ L +L G V AS G LR C T A+K C + TT C G C + +  
Sbjct: 7 LLLWMLLSVGGVW-ASRGPLRPL--CRPINATLAAEKEACPICITFTTSICAGYCPSMVR 63

Query: 208 PILEPPYIEAHHR-VCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378  
+ P + A + VCTY E + +++LP C PGVDP ++PVA+ C CG C TT+  
Sbjct: 64 VM--PAALPAIPQPVCTYRELRFASIRLPGCCPPGVDPMVSPVALSCHCGPCQIKTTD 119

### ClustalW alignment for NOVGON:

[illegible]

### Figure 9A

#### NOVINTRA A cDNA sequence:

Regions 116708 to 116812 (1-105bp), 117121 to 117248 (106-233p), and 117529 to 117778 (234-483bp).

CACTGTCATACTGTTTCAGAATTAAATATGCAGACCAGAAGGCTCTATACACAAGAG  
ATGGCCAGCTGCTGGTGGGAGATCCTGTTGCAGACAACCTGCTGTGCAGAGAAGATC  
TGCATACTTCCTAACAGAGGCTTGGCCCGCACCAAGGTCCCCATTTTCCTGGGGATC  
CAGGGAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCTTCCCTACA  
GCTGGAGCCATCCACCTTGCCCCCACAGGATGTGAACATTGAGGAACTGTACAAAG  
GTGGTGAAGAGGCCACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCA  
GGCTTGAGGCTGCTGCCTGGCCTGGCTGGTTTCCTGTGTGGCCCGGCAGAGCCCCAGC  
AGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTTTTACTTTG  
AACAGAGCTGGTAGGGAGACAGGAAACTGC

### Figure 9B

#### NOVINTRA A Protein sequence:

LSYCFRIKYADQKALYTRDGQLLVGDPVADNCCAEEKICILPNRGLARTKVPIFLGIQGG  
RCLACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWP  
GWFLCGPAEPQQPVQLTKESEPSARTKFYFEQSW

## Figure 10A

### BlastN for NOVINTRA A:

gb:GENBANK-ID:AF072476|acc:AF072476 Equus caballus interleukin-1 receptor  
antagonist secretory form (IL-1ra) gene, partial cds - Equus caballus,  
221

bp

Top Previous Match Next Match

Length = 221

Plus Strand HSPs:

Score = 321 (48.2 bits), Expect = 8.1e-08, P = 8.1e-08  
Identities = 147/218 (67%), Positives = 147/218 (67%), Strand = Plus / Plus

Query: 253 AGGATGTGAACATTGAGGAACTGTACAA-AGGTGGTGAAGAGGCCACACGCTTCACCTTC 311  
AGG GT AACAT GA CTG CAA A G GA GAG CA CGCTTCACCTTC

Sbjct: 4 AGGCAGTTAACATCACTGACCTGAGCAAGAACAAG-GAGGAGAACAAGCGCTTCACCTTC 62

Query: 312 TTCCAGAGCAG-CTCAGGCTCCGCCTTCAGGCTT-GAGGCTGCTGCCTGGCCTGGCTGGT 369  
TCC G CA C GGC CC CC CAG CTT GAG CTGC GCCTG CCTGGCTGGT

Sbjct: 63 ATCC-GCTCAAACAGTGGCCCCACCACCAG-CTTCGAGTCTGCCGCCTGCCCTGGCTGGT 120

Query: 370 TCCTGTGTGGCCCGGCAG-AGCCCCAGCAGCCAGTACAGC-TCACCAAGGAG---AGTGA 424  
TCCT TG CG CAG AG C A C GCC GT CAGC TCACCAA AG A GA

Sbjct: 121 TCCTCTGCACGGCG-CAGGAGGCAGACCGGCCCGT-CAGCCTCACCAACAAGCCCCAAAGA 178

Query: 425 GCCCT-CAGCCCGT-ACCAAGTTTTACTTTGAACAGAGCTGGTAG 467

G CCT CA GT ACCAAGTT TACTT A AG C GTAG

Sbjct: 179 GTCCTTCATG--GTCACCAAGTTCTACTTCCAGGAGGACCAGTAG 221

Figure 10B

**BlastX for NOVINTRA A:**

ptnr:TREMBLNEW-ACC:CAB59831 IL-1L1 PROTEIN - Mus musculus (Mouse), 155 aa.  
Top Previous Match Next Match  
Length = 155

Plus Strand HSPs:

Score = 309 (108.8 bits), Expect = 8.0e-27, P = 8.0e-27  
Identities = 70/149 (46%), Positives = 93/149 (62%), Frame = +3

```
Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188
      CFR+K + K LY + QLL G A+ E+I ++PNR L + P+ LG+QGG+C
Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAEKVIKGEEISVVPNRALDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGEEATRFTFFQSSSGSAFRLEAAAWPGW 368
      L+C TE+GP L+LEP VNI ELY G +E+ FTF++ G E+AA+PGW
Sbjct: 68 LSC-GTEKGPIKLKLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458
      FLC E QPV+LT+ E A T FYF+Q
Sbjct: 120 FLCTSPEADQPVRLTQIPEDPAWDAPITDFYFQQ 153
```

>ptnr:SPTREMBL-ACC:Q9UBH0 FIL1 DELTA (INTERLEUKIN-1 LIKE PROTEIN 1)  
(INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG 1) (INTERLEUKIN-1 DELTA) - Homo  
sapiens (Human), 155 aa.

Plus Strand HSPs:

Score = 285 (100.3 bits), Expect = 4.3e-24, P = 4.3e-24  
Identities = 67/149 (44%), Positives = 89/149 (59%), Frame = +3

```
Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188
      CFR+K + K LY + QLL G A E+I ++PNR L + P+ LG+QGG+C
Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAGKVIKGEEISVVPNRWLDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGEEATRFTFFQSSSGSAFRLEAAAWPGW 368
      L+C +E P+L LEP VNI ELY G +E+ FTF++ G E+AA+PGW
Sbjct: 68 LSCGVGQE-PTLTLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458
      FLC E QPV+LT+ E T FYF+Q
Sbjct: 120 FLCTVPEADQPVRLTQLPENGGWNAPITDFYFQQ 153
```

Figure 11

# ClustalW for NOVINTRA A:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

## Sequences used:

- 1) X86458spoil1 (cDNA encoding a human spoil-I protein); X86459spoil2 (cDNA encoding a human spoil-II protein); X89432-il1delta (human IL-1 delta encoding cDNA); Q14628 (intracellular IL-1 receptor antagonist type II-human); G512010il1beta (ovine IL-1 beta - pig)

```

X86458spoil1  - - - - - DNHTMRGTPGDA - - - - - DGG - - GRAVYQS - - - - -
X86459spoil2  - - - - - DNHTMRGTPGDA - - - - - DGG - - GRAVYQS SESNAVGMGLWRLRPSALTLSPV
X89432-il1delta - - - - - MALADLYEEG - - - - - GGG - - GGEGEDNADSK - - - - - E - - - - -
Q14628        - - - - - MALADLYEEG - - - - - GGG - - GGEGEDNADSK - - - - - E - - - - -
il1beta-1DNA  - - - - - MALADLYEEG - - - - - GGG - - GGEGEDNADSK - - - - - E - - - - -
G512010il1beta MATVPEP INEVMAYYSDENELLFEV DGP KQMK SCT QHLDLGSMGDGN IQLQISHQLYNKS

X86458spoil1  - - - - - MCKPITGT INDLNQVWTLQGQNLVAVPRSDS - - VTPVTVAVIT
X86459spoil2  EAPAFSAPLCTLPFPVCKPITGT INDLNQVWTLQGQNLVAVPRSDS - - VTPVTVAVIT
X89432-il1delta - - - - - MVLSGALCFRMD SALKVLYLHNNQLLAGGLHA - - - CKVIKGEET
Q14628        - - - - - TICRPSGRKSSKMQAFRIWDVNQKTFYLRNNQLVAGYLQG - - - PNVNLEEKI
il1beta-1DNA  - - - - - GPSALSYCFRIKYADQKALYTRDGLLVGDPVA - - - DNCCAETKI
G512010il1beta FRQVVSIVAMEKLRSRAYEHVFRDDDLRSILSFIIFEEEPVIFETSSDELECDAAVQSVK

X86458spoil1  CKYPEAL - - - - - EQGRGDPIYLGIONPEM
X86459spoil2  CKYPEAL - - - - - EQGRGDPIYLGIONPEM
X89432-il1delta SVVPNRW - - - - - LDASLSPVILGVGGGSQ
Q14628        DVVP - - - - - IEPHALFLGIHGGKM
il1beta-1DNA  CILPNRG - - - - - LARTKVPIFLGIQGGSR
G512010il1beta CKLQDR EQKSLVLDSPCVLKALHL L SQEMSREVVFCMSFVQGE ERDNKIPVALGIRDKNL

X86458spoil1  CLYCEKVGEQPTLQLKE - - - - - QKIMDLYGQPEPVKPFLLFYRAKT GRTSTLESVAFPD
X86459spoil2  CLYCEKVGEQPTLQLKE - - - - - QKIMDLYGQPEPVKPFLLFYRAKT GRTSTLESVAFPD
X89432-il1delta CLSCG-VGQEP TLTLEP - - - - - VNIMELYLGAKESKSFTFYRRDMGLTSSSFESAAYPG
Q14628        CLSCVKSGDETRLQLEA - - - - - VNIITDLSNRKQDKRFAFIRSDSGPTTSFESAACPG
il1beta-1DNA  CLACVETE EGPSLQLEPSTLPPQD VNIIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWPG
G512010il1beta YLSCVKK GDTPTLQLEE - - - - - VDPKVYPKRNMERFVFYKTEIKNTVEFESVLYPN

X86458spoil1  WFIASS - KRDQPIILTSSELGKS - - - - YNTAFELNIND -
X86459spoil2  WFIASS - KRDQPIILTSSELGKS - - - - YNTAFELNIND -
X89432-il1delta WFLCTVPEADQPVRLTQLPENGGWNAPIITDFYFQQCD -
Q14628        WFLCTAMEADQPVSLTNMPDEG - - - - VMYTKFYFQED -
il1beta-1DNA  WFLCGPAEPQQPVQLTKSEPS - - - - ARTKFYFEQSW -
G512010il1beta WYISTSQIEEKPVFLGRFRGGQ - - - - DITDFRMETLSP

```

### Figure 12A

#### NOVINTRA B cDNA sequence:

Regions 116968 to 117028 (1-61bp), 104067 to 104164 (62-159bp), 101958 to 102098 (160-300bp), and 100915 to 101134 (301-520bp) of genomic clone (-frame).

ATGGGCACACCTGGCCTGGCCCTGCATGCAGACTGGACGGTGAGCCAGGACTTCTG  
CAGGACACCCAAATCCTATGCTATTCGTGATTCTCGACAGATGGTGTGGGTCCTGAG  
TGGAATTCTTTAATAGCAGCTCCTCTTAGCCGCAGCATTAAGCCTGTCACTCTTCAT  
TTAATAGCCTGTAGAGACACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTA  
CCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC  
TACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC  
AGAAGCCCTTTCTCTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTTTCAGTCAGT  
CTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAGGACAGCCCATCTTTCTC  
ACCAAGGAGAGAGGCATAACTAATAACACTAACTTCTACTTAGATTCTGTGGAATA  
AATCCAGC

### Figure 12B

#### NOVINTRA B Protein sequence:

MGTPGLALHADWTVSQDFCRTPKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLI  
ACRDTEFSDKEKGNMVYLGKGDLCFCAEIQ GKPTLQLKEKNIMDLYVEKKAQKPFL  
FFHNKEGSTSVFQSVSPGWFIATSTTSGQPIFLTKERGITNNTNFYLDSE



Figure 13A

**BlastN for NOVINTRA B:**

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,  
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Plus Strand HSPs:

Score = 309 (46.4 bits), Expect = 1.1e-07, P = 1.1e-07

Identities = 197/331 (59%), Positives = 197/331 (59%), Strand = Plus / Plus

Query: 169 CATTTAATAGCCTGTA-GAGAC-ACAGAATTCAGTGACAAGGAAAAGGTAATATGGTTT 226  
CA TA TA CTG A GAG A AGA T GTG C G AG T AT T GT T  
Sbjct: 217 CAAATACTAAACTGGAAGAGAAGATAGATGTG-GTGCCT--GTTGAGCCTCATTTTGTGT 273

Query: 227 ACCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC-T 285  
CCTGGG ATC A GGA A CT TG CT T CTGTG AA T C GG A G T  
Sbjct: 274 TCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCTCTGTGTC-AAGT-CTGGTGATGAGAT 331

Query: 286 -ACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC-AGA 343  
A T CAG T A G A AA ATCA GACCTG A GA AG AGCA A A  
Sbjct: 332 GAAGCTCCAGTTGGACGCAGTTAACATCACAGACCTG-AGAAAGAACAGCGAGCAGGACA 390

Query: 344 AGCCCTTTCTCTTTTCCACAATAA-AGAAGGCTCCACTTCTGTCTTTTCAGTCAGTCTCT 402  
AGC CTT CTT TCC C A AG GGC CCAC C CTTT AGTCAG C C  
Sbjct: 391 AGCGCTTCACCTTCATCCGCTCCGACAGT-GGCCCCACACAGCTTTGAGTCAGCCGCC 449

Query: 403 TACCCTGGCTGGTTTCATAGCCACCTCCACCACAT-CAGGACAGCCCATCTTTCTCACCAA 461  
T CCTGGCTGGTTC T CAC T CAC A A CAG CAGCC T CTCACCAA  
Sbjct: 450 TGTCCTGGCTGGTTTCCTCTGCAC-TGCACTAGAGGCAGACCAGCCTGTTGGCCTCACCAA 508

Query: 462 GGAGAG-AG-GCATAACT-AATAACACTAACTTCTACTT 497  
G A GCA T AA CAC AA TTCTACTT  
Sbjct: 509 CACGCCCAAAGCAGCCGTCAAGGTCACCAAGTTCTACTT 547

Figure 13B

**BlastX for NOVINTRA B:**

>ptnr:SPTREMBL-ACC:Q9UHA5 FIL1 ETA - Homo sapiens (Human), 157 aa.

Plus Strand HSPs:

Score = 777 (273.5 bits), Expect = 3.2e-76, P = 3.2e-76

Identities = 149/149 (100%), Positives = 149/149 (100%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 243

PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK

Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 423

KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA

Sbjct: 69 KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 128

Query: 424 TSTTSGQPIFLTKEGKITNNTNFYLDSE 510

TSTTSGQPIFLTKEGKITNNTNFYLDSE

Sbjct: 129 TSTTSGQPIFLTKEGKITNNTNFYLDSE 157

>ptnr:SPTREMBL-ACC:Q9NZH7 INTERLEUKIN-1 HOMOLOG 2 - Homo sapiens (Human), 164 aa.

Plus Strand HSPs:

Score = 411 (144.7 bits), Expect = 1.9e-37, P = 1.9e-37

Identities = 80/85 (94%), Positives = 81/85 (95%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 243

PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK

Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMD 318

KDLCLFCAEIQGKPTLQLK + D

Sbjct: 69 KDLCLFCAEIQGKPTLQLKLQGSQD 93

>ptnr:TREMBLNEW-ACC:AAF02757 INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG  
- Homo sapiens (Human), 155 aa.

Top Previous Match Next Match

Plus Strand HSPs:

Score = 197 (69.3 bits), Expect = 5.9e-15, P = 5.9e-15

Identities = 52/147 (35%), Positives = 76/147 (51%), Frame = +1

Query: 73 YAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGKDL 252

+ ++DS V L N L+A L K + I+ + D ++ LG++G

Sbjct: 9 FRMKDSALKVLYLHNNQLLAGGLHAG-KVIKGEISVVPNRWLDASLSPVI-LGVQGSQ 66

Query: 253 CLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIATST 432

CL C Q +PTL L+ NIM+LY+ K K F F+ G TS F+S +YPGWF+ T

Sbjct: 67 CLSCGVGQ-EPTLTLEPVNIMELYLGAKESKSFTFYRRDMGLTSSSFESAAYPGWFLCTVP 125

Query: 433 TSGQPIFLTKEGKITNNTNFYLDSE 510

+ QP+ LT+ E G N T+FY +

Sbjct: 126 EADQPVRILTQLPENGGWNAPITDFYFQCD 155

Figure 14

# ClustalW for NOVINTRA B:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (*e.g.* L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

## Sequences used:

- 2) X86459spoil2 (cDNA encoding a human spoil-II protein; Q14628 (intracellular IL-1 receptor antagonist type II-human); AAF02757 (intracellular IL-1 receptor antagonist type II-human); G512010; (OVINE IL-1 BETA - Pig)

## Multiple Alignment:

```

il1beta2DNA      - - - - - MGTPGLALHADWTVSQD - - - - -
X86459spoil2     - - - - - DNHTMRGTPGDADGGGRAVYQSSESN
Q14628           - - - - - MALADLYEEGGGGGGEDEDNADSKE -
AAF02757         - - - - -
G512010il1beta  MATVPEPINEVMAYYSDENELLEFVDGPKQMKSC TQHLDLGSMEDGNIQLQISHQLYNKS

il1beta2DNA      - - - - - FCRT - - - - - PKSYAIR - - - - -
X86459spoil2     AVGMGLWRLRPSALTLPVEAPAFSAPLCTLPFPVPCK - PITGTIN - - - - -
Q14628           - - - - - TICRPSGRKSSK - MQAFRIW - - - - -
AAF02757         - - - - - - MVLSG - ALCFRMK - - - - -
G512010il1beta  FRQVVSIVAMEKLRSRAYEHVFRDDDLRSILSFIFEEEPVIFETSSDELLCDAAVQSVK

il1beta2DNA      - - - - - DSRQMWWVLSGNSLLIAPLSRSIKPVTLHLIACRDTEFSDK - EKGNMVYLGIKCKD
X86459spoil2     - - - - - DLNQQVWTLQGQNLVAVPRSDSVTPVTVAVITCKYPEALEQ - GRGDPITYLGIQNPE
Q14628           - - - - - DVNQKTEYLRRNNQLVAGYLO - GPNVNLEEKIDVVP - - - - - IEPHALFLGIHCGK
AAF02757         - - - - - DSALKVLYLHNNQLLAGGLH - AGKVIKGEESVVPNRWLD - ASLSPVILGVQGG
G512010il1beta  CKLQDREOKSLVLDSPCVLKAHLHLSQEMSREVVFCMSFVQGEERDNKIPVALGIRDKN

il1beta2DNA      LCLFCAELQGKPTLQLKEKNIMDLVVEKKAQKPFLEFHNKEGSTSVFQSVSYPGWFIATS
X86459spoil2     MCLYCEKVGEQPTLQLKEQKIMDLYGQPEPVKPFLEFYRAKTGRSTLTESVAEPDWFIASS
Q14628           MCLSCVKSGDETRLQLEAVNITDLSNRKQDKRFAFIRSDSGPTTTSFESAACPWFLECTA
AAF02757         QCLSCG - VGQEPFTLTLEPVNIMELYLGAKESKSFTFYRRDMGLTSSSFESAAYPGWFLECTV
G512010il1beta  LYLSCVKKGGDTPTLQLEEVDPKVYP - KRNMEKRFVFYKTEIKNTVEFESVLYPNWYIST

il1beta2DNA      TTSGQPIFLTKER - - G - - ITNNTNFYLDSE -
X86459spoil2     KRD - QPIILTSEL - - G - - KSYNTAFELNIND -
Q14628           MEADQPVS LTNMPDEG - - - - - VMVTKFYFQEDE -
AAF02757         PEADQPVRLTQLPENGGWNAPIITDFYFQQCD -
G512010il1beta  QIEEKPVFLGRFR - - G - - GQDITDFRMETLSP

```

### Figure 15A

#### NOVINTRA C cDNA sequence:

Region 168700 to 168880 (1-181bp), 169967 to 170118 (182-331bp) and 170635 to 170694 (332-391bp) of the genomic clone (- frame).

```
GATATCAATCATCGGGTGTGGGTTCCTTCAGGACCAGACGCTCATAGCAGTCCCGAGG
AAGGTGTTCCCGAGTCACTATTGCCTTAATCTCATGCCGACATGTGGAGACCCTTGAG
AAAGACAGAGGGAACCCCATCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGAT
GTGTGCTAAAGTCGGGGACCAGCCACACTGCAGCTGAAGCTTCAGGAAAAGGATA
TAATGGATTTGTACAACCAACCCGAGCCTGTGAAGTCCTTTCTCTTCTACCACAGCC
AGAGTGGCAGGAACCTCCACCTTCGAGTCTGTGGCTTTCCTGGGTGGTTCATCGCTG
TCAGCTCTGAAGGAGGCTGTCCTCTCATCCTTACCCAAGAACTGGGGAAAG
```

### Figure 15B

#### NOVINTRA C Protein sequence:

```
DINHRVWVLQDQTLIAVPRKVPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCLMCAK
VGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEGGC
PLILTQELGK
```

Figure 16A

**BlastN for NOVINTRA C:**

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,  
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Minus Strand HSPs:

Score = 274 (41.1 bits), Expect = 5.6e-06, P = 5.6e-06

Identities = 150/244 (61%), Positives = 150/244 (61%), Strand = Minus / Plus

Query: 258 TCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGATGTGTGCTAAAGTCGGG-GACCAG 200  
T T CCTGGG T ATGGA AA CT TGCCTG TGTG T AAGTC GG GA AG  
Sbjct: 271 TGTTCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCCTGTG-TCAAGTCTGGTGATGAG 329

Query: 199 CCCACACTGCAGCTGAAGCTTCAGGAAAAGGATATAATGGATTTGTACAACCAACC-CGA 141  
A CT CAG TG A C CAG AA AT A GA TG A AA AAC CGA  
Sbjct: 330 ATGAAGCTCCAGTTGGA-CG-CAGTTAAC---ATCACAGACCTG-AGAAAGAACAGCGA 382

Query: 140 GCCTGTGAAGTCCTTTCTCTTCTACCACAGCCAGAGTGGCAGGAACTCCACCTTCGAGTC 81  
GC G AAG CTT CTTC CC C C A AGTGGC A C CCA CTT GAGTC  
Sbjct: 383 GCAGGACAAGCGCTTCACCTTCATCCGCTCCGACAGTGGCCCCACCACCAGCTTTGAGTC 442

Query: 80 TGTGGCTTTCCCTGGCTGGTTTCATCGCTGT-CAGCTCTGAAGG-AGGCTGTCCTCTCATC 23  
G GC T CCTGGGTGGTTC TC TG C GC CT AGG AG C CCT T C  
Sbjct: 443 AGCCGCTGTCTCTGGCTGGTTTCCTC--TGCACTGCACTAGAGGCAGACCAGCCTGTTGGC 500

Query: 22 CTTACCCA 15  
CT ACC A  
Sbjct: 501 CTCACCAA 508

Figure 16B

**BlastX for NOVINTRA C:**

>ptnr:SPTREMBL-ACC:Q9UHA7 FIL1 EPSILON - Homo sapiens (Human), 158 aa.  
Plus Strand HSPs:

Score = 646 (227.4 bits), Expect = 2.4e-62, P = 2.4e-62  
Identities = 126/130 (96%), Positives = 127/130 (97%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 174  
DINHRVWVLQDQTLIAVPRK + PVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC  
Sbjct: 17 DINHRVWVLQDQTLIAVPRKDRMSPTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 76

Query: 175 AKVGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEG 354  
AKVGDQPTLQLK EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEG  
Sbjct: 77 AKVGDQPTLQLK--EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEG 134

Query: 355 GCPLILTQELGK 390  
GCPLILTQELGK  
Sbjct: 135 GCPLILTQELGK 146

>ptnr:SPTREMBL-ACC:Q9NZH8 INTERLEUKIN-1 HOMOLOG 1 - Homo sapiens, 169 aa.

Plus Strand HSPs:

Score = 416 (146.4 bits), Expect = 5.7e-38, P = 5.7e-38  
Identities = 82/130 (63%), Positives = 101/130 (77%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 174  
D+N +VW LQ Q L+AVPR V PVT+A+I+C++ E LE+ RG+PIYLG+ +CL C  
Sbjct: 29 DLNQQVWTLQGQNLVAVPRSDSVTPVTAVITCKYPEALEQGRGDPIYLGIONPEMCLYC 88

Query: 175 AKVGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEG 354  
KVG+QPTLQLK E+ IMDLY QPEPVK FLFY +++GR ST ESVAFP WFIA SS+  
Sbjct: 89 EKVGEQPTLQLK--EQKIMDLYGQPEPVKPFIFYRAKTGRTSTLESVAFPDWFIA--SSKR 145

Query: 355 GCPLILTQELGK 390  
P+ILT ELGK  
Sbjct: 146 DQPIILTSELGK 157

>ptnr:SWISSPROT-ACC:P25085 INTERLEUKIN-1 RECEPTOR ANTAGONIST PROTEIN  
PRECURSOR (IL-1RA) (IL-1RN) (IRAP) - Mus musculus (Mouse), 178 aa.

Top Previous Match Next Match

Minus Strand HSPs:

Score = 173 (60.9 bits), Expect = 2.1e-12, P = 2.1e-12  
Identities = 35/81 (43%), Positives = 50/81 (61%), Frame = -1

Query: 259 IYLGLNGLNLCCLMCAKVGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFES 80  
++LG++G LCL CAK GD ++L+L+E +I DL E K F F S+ G ++FES  
Sbjct: 82 VFLGIHGGKLCCLSCAKSGDD--IKLQLEEVNITDLSKNKEEDKRFTFIRSEKGPSTSFES 139

Query: 79 VAFPGWFIAVSSEGGCPLILT 17  
A PGWF+ + E P+ LT  
Sbjct: 140 AACPGWFLCTTLEADRPVSLT 160

Figure 17

# ClustalW for NOVINTRA C:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

## Sequences used:

- 1) IL1X\_MOUSE: Locus - IL1X\_MOUSE; Accession - P25085; PID - g124313
- 2) IL1X\_HORSE: Locus - IL1X\_HORSE; Accession - O18999; PID - g6166230
- 3) AAF02757\_HUMAN: Locus - AF186094\_1; Accession - AAF02757; PID - g6049805

```

IL1X_MOUSE      MEICWGPYSHLISLLILLFHSEAACRPSGKRPCCKMQAFRIWDINQKTFYLRNNQLIAGY
IL1X_HORSE      MEIRRRSVRHLIS-LLLFIFYSETACHPLGKRPCCKMQAFRIWDVYNQKTFYMRNNQLVAGY
AAF02757_Human  -----MVLSGALC-----FRMKDSALKVLYLHNNQLLAGG
Novel_IL1       -----DINHRVWVLQDQTLIAPV

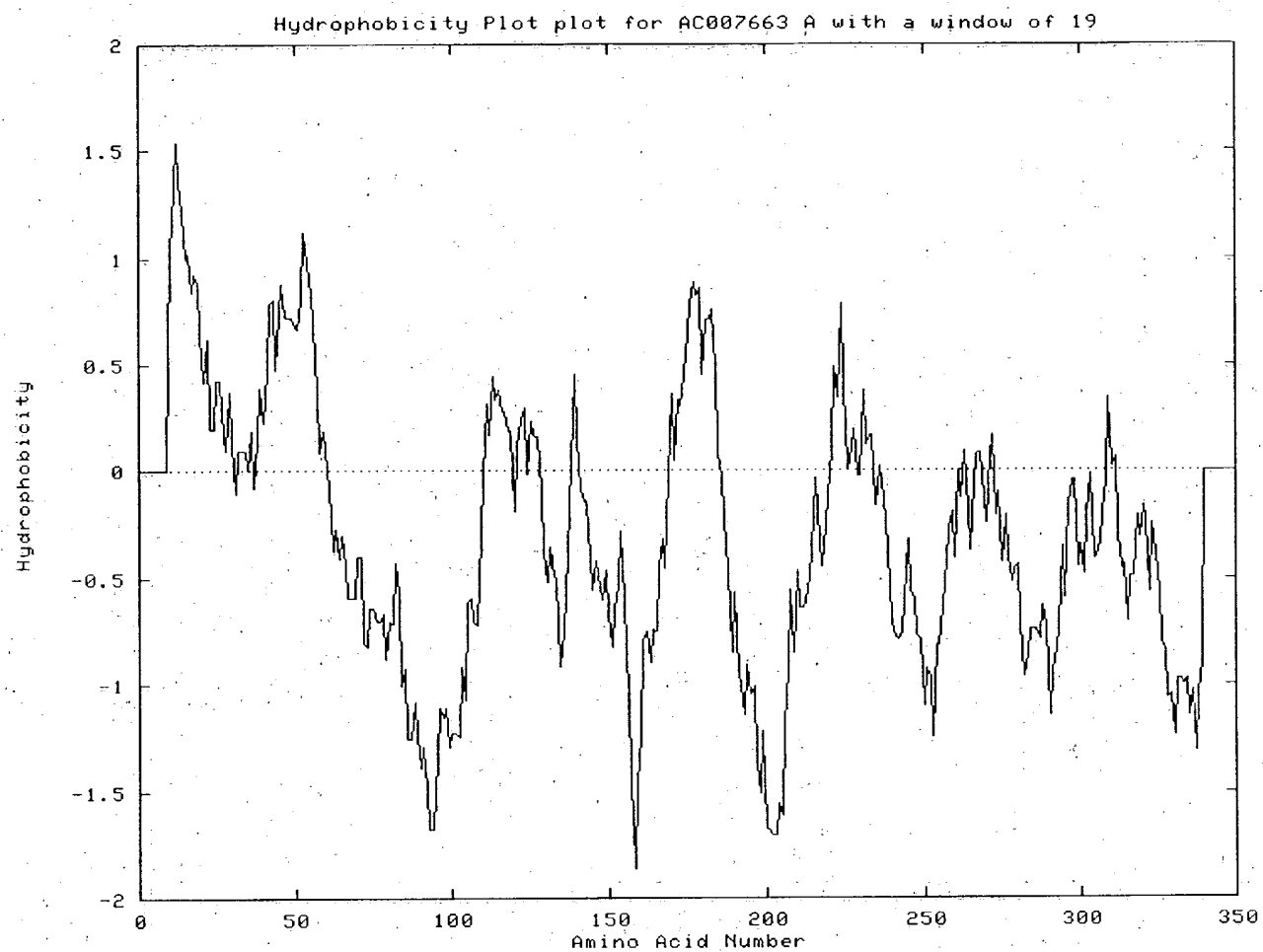
IL1X_MOUSE      LGGPNIKLE---EKIDMVP-----IDLHSVFLGIHGGKLCLSCAKSGDDIKLQLEEVN-
IL1X_HORSE      LQESNTKLO---EKIDVVP-----IEPDALFLGLHGRKLCLACVKSGDEIRFQLEAVN-
AAF02757_Human  LHAGKVIKG---EEISVVPNRWLDASLSPVILGVQGGSCQLSCG-VGQEP TLTLEPVN-
Novel_IL1       RKVFPVTIALISCRHVETLEK---DRGNPIYLG-NGLNLC LMCAKVGDOPTLQLKLQEK

IL1X_MOUSE      -ITDLSKNKEEDKRFTFIRSEKGPTTSFESAACPGWFLCTTLLEADRPVSLTNTPEE---P
IL1X_HORSE      -ITDLSKNKEENKRFTFIRSN SGPTTSFESAACPGWFLCTAQEADRPVSLTNKPKE---S
AAF02757_Human  -IMELYLGAKESKSFTFYRRDMGLTSSSFESAAYPGWFLCTVPEADQPVRLTQLPENGGWN
Novel_IL1       DIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFFPGWFIAVSSSEGGLPLILTQELGK---

IL1X_MOUSE      LITVKFYFQEDQ
IL1X_HORSE      FMVTKFYLQEDQ
AAF02757_Human  APITDFYFQQCD
Novel_IL1       -----

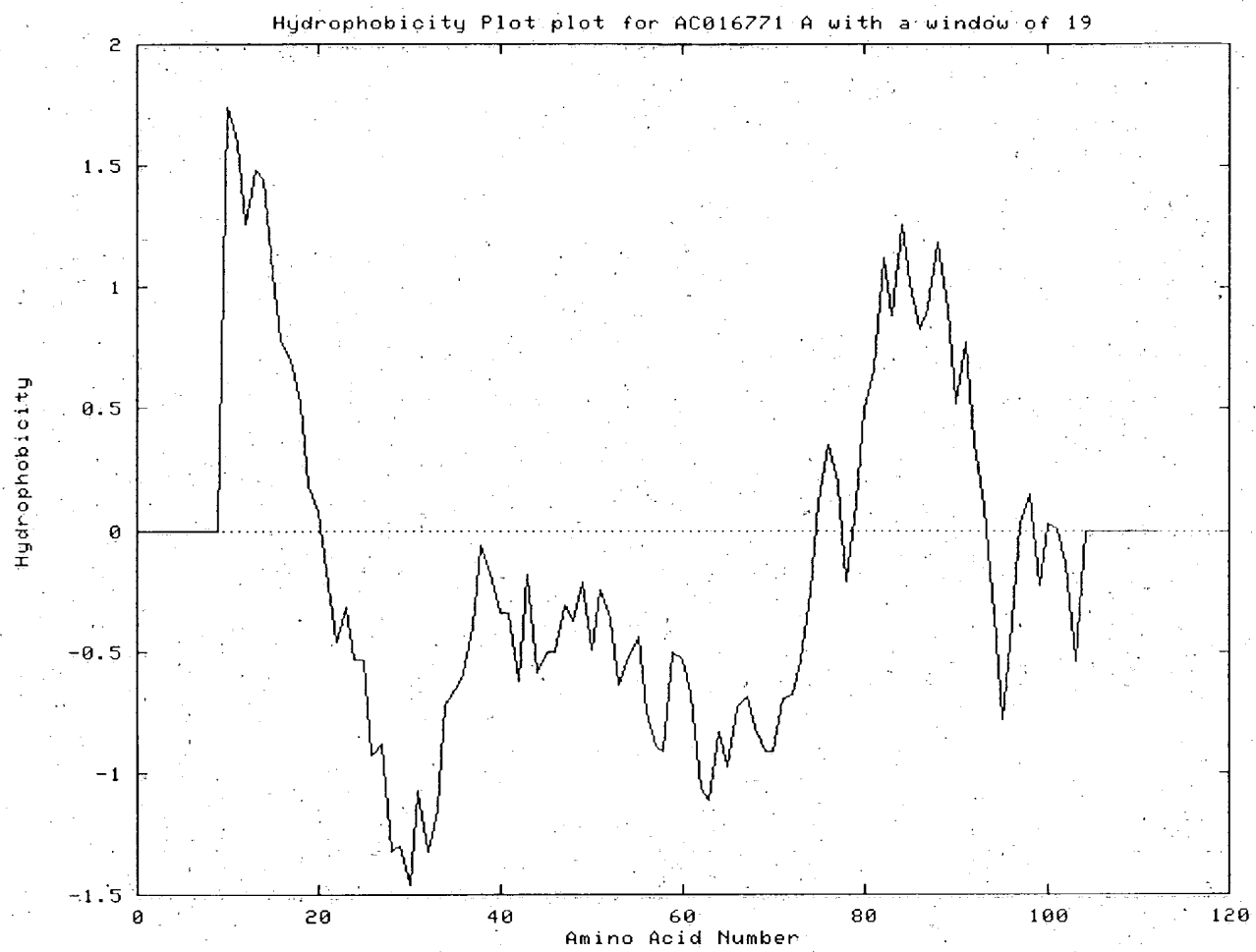
```

**Figure 18**

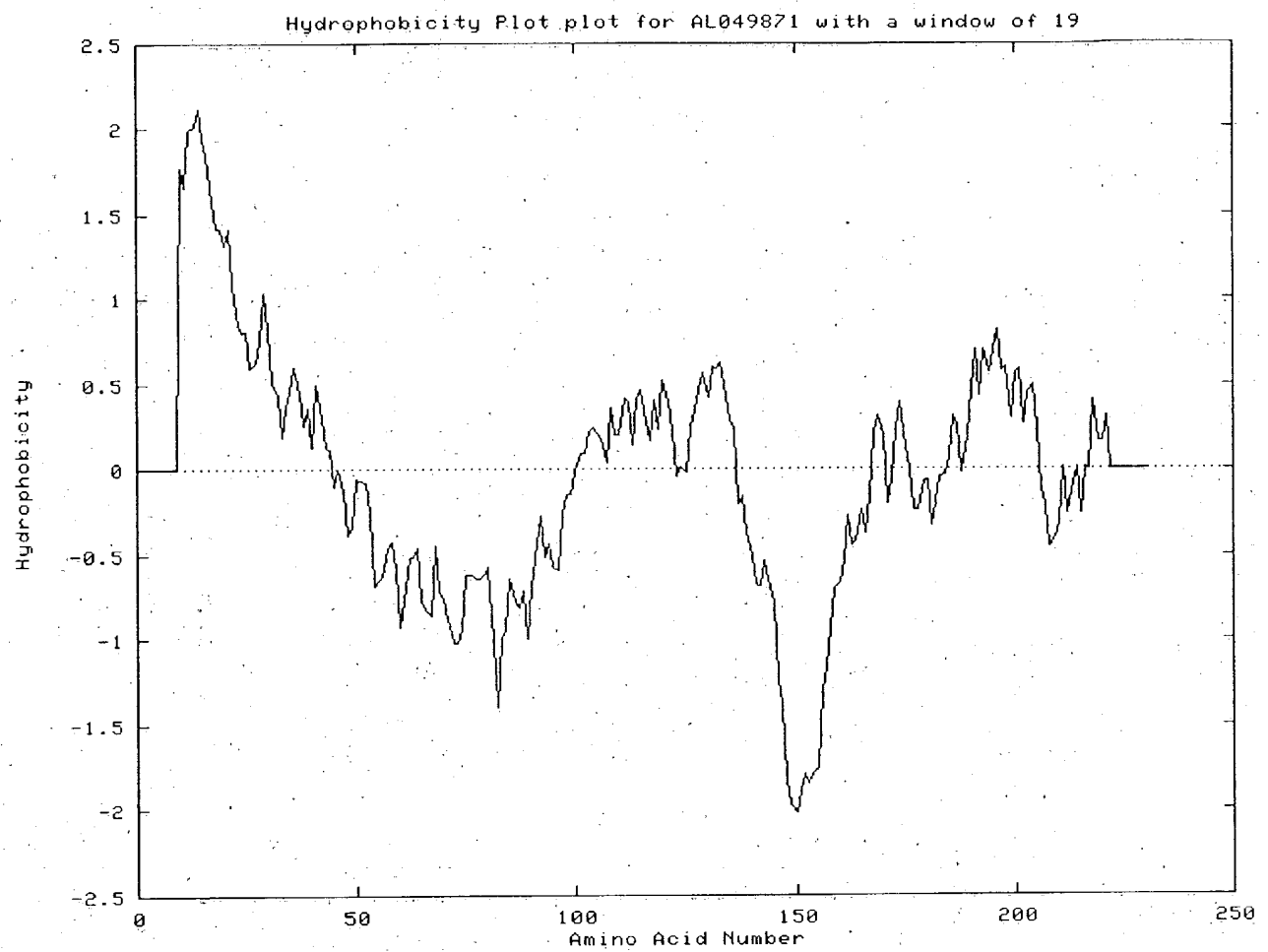




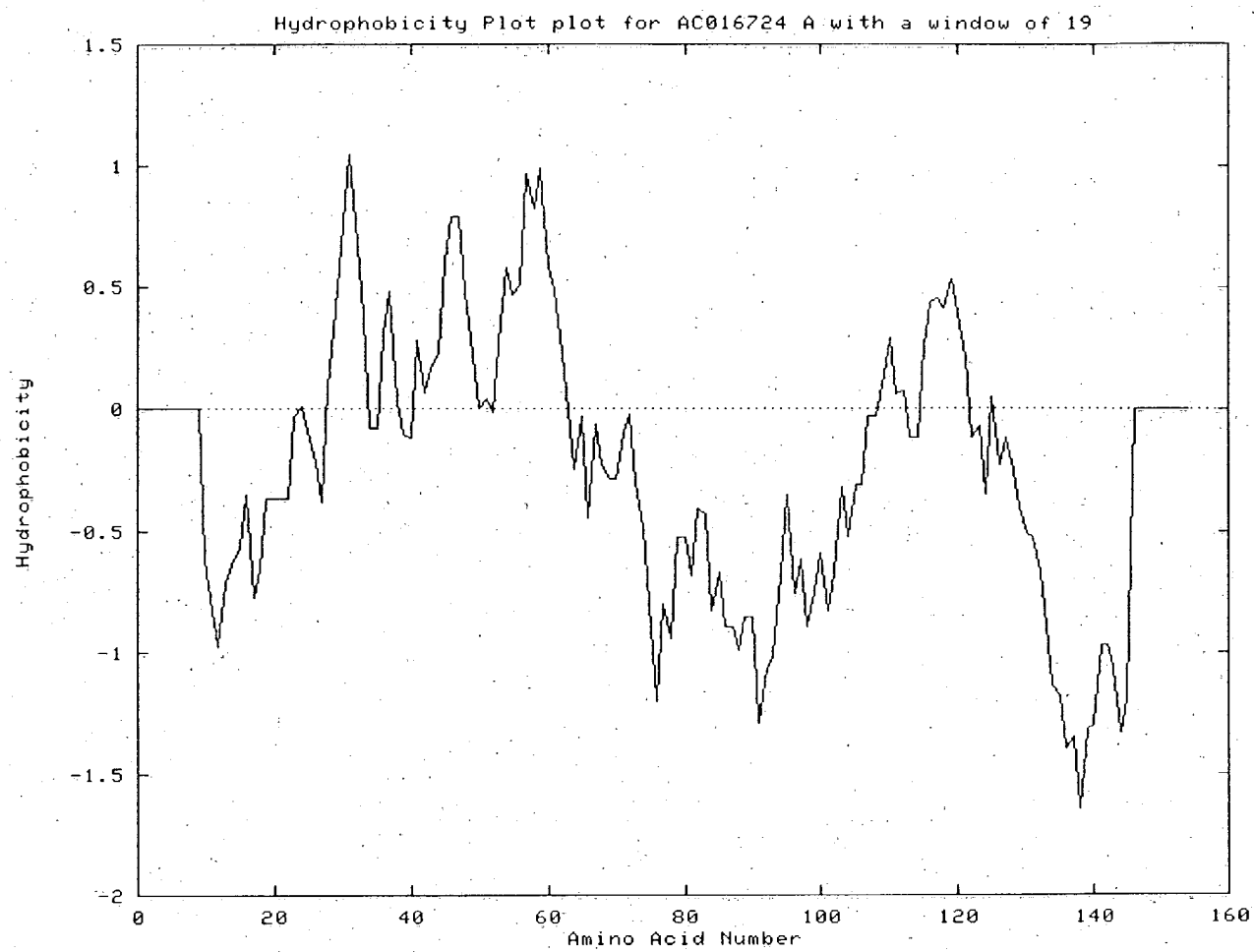
**Figure 19**



**Figure 20**



**Figure 21**



**Figure 22**

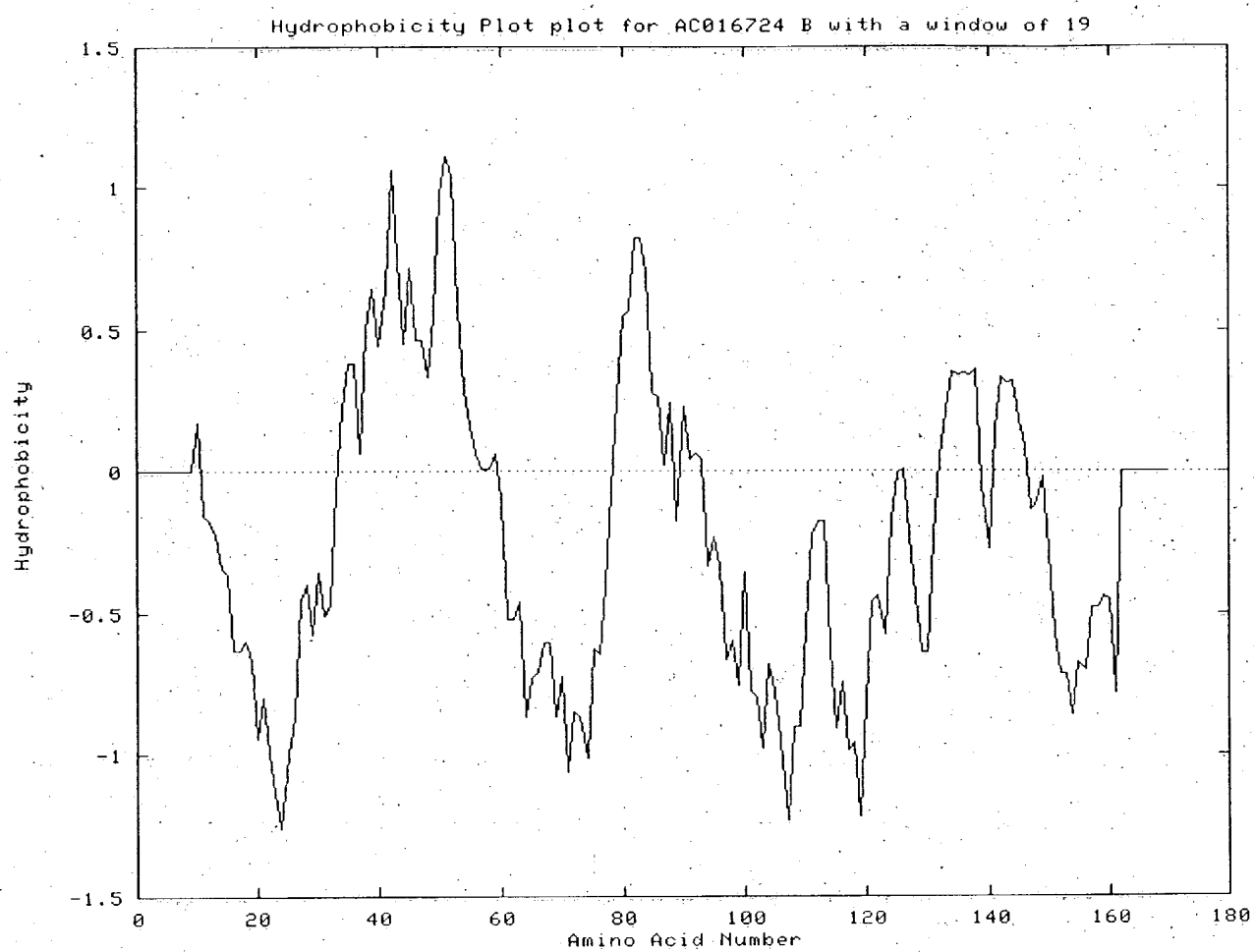


Figure 23

